EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S1	589	(548/950).CCLS.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2007/05/31 12:34
S2	341	(548/953).CCLS.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2007/05/31 12:35
S3	2243	(514/422).CCLS.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2007/05/31 12:41
S4	726	(548/527).CCLS.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2007/05/31 12:35
S5	6	(("5495046") or ("6437165") or ("20020042443")).PN.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2007/05/31 12:41

```
Connecting via Winsock to STN


Welcome to STN International!  Enter x:x

LOGINID:SSSPTA1600RXA

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1          Web Page for STN Seminar Schedule - N. America
 NEWS  2  JAN 08  CHEMLIST enhanced with New Zealand Inventory of Chemicals
 NEWS  3  JAN 16  CA/CAplus Company Name Thesaurus enhanced and reloaded
 NEWS  4  JAN 16  IPC version 2007.01 thesaurus available on STN
 NEWS  5  JAN 16  WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
 NEWS  6  JAN 22  CA/CAplus updated with revised CAS roles
 NEWS  7  JAN 22  CA/CAplus enhanced with patent applications from India
 NEWS  8  JAN 29  PHAR reloaded with new search and display fields
 NEWS  9  JAN 29  CAS Registry Number crossover limit increased to 300,000 in
                  multiple databases
 NEWS 10  FEB 15  PATDPASPC enhanced with Drug Approval numbers
 NEWS 11  FEB 15  RUSSIAPAT enhanced with pre-1994 records
 NEWS 12  FEB 23  KOREAPAT enhanced with IPC 8 features and functionality
 NEWS 13  FEB 26  MEDLINE reloaded with enhancements
 NEWS 14  FEB 26  EMBASE enhanced with Clinical Trial Number field
 NEWS 15  FEB 26  TOXCENTER enhanced with reloaded MEDLINE
 NEWS 16  FEB 26  IFICDB/IFIPAT/IFIUDB reloaded with enhancements
 NEWS 17  FEB 26  CAS Registry Number crossover limit increased from 10,000
                  to 300,000 in multiple databases
 NEWS 18  MAR 15  WPIDS/WPIX enhanced with new FRAGHITSTR display format
 NEWS 19  MAR 16  CASREACT coverage extended
 NEWS 20  MAR 20  MARPAT now updated daily
 NEWS 21  MAR 22  LWPI reloaded
 NEWS 22  MAR 30  RDISCLOSURE reloaded with enhancements
 NEWS 23  APR 02  JICST-EPLUS removed from database clusters and STN
 NEWS 24  APR 30  GENBANK reloaded and enhanced with Genome Project ID field
 NEWS 25  APR 30  CHEMCATS enhanced with 1.2 million new records
 NEWS 26  APR 30  CA/CAplus enhanced with 1870-1889 U.S. patent records
 NEWS 27  APR 30  INPADOC replaced by INPADOCDB on STN
 NEWS 28  MAY 01  New CAS web site launched
 NEWS 29  MAY 08  CA/CAplus Indian patent publication number format defined
 NEWS 30  MAY 14  RDISCLOSURE on STN Easy enhanced with new search and display
                  fields
 NEWS 31  MAY 21  BIOSIS reloaded and enhanced with archival data
 NEWS 32  MAY 21  TOXCENTER enhanced with BIOSIS reload
 NEWS 33  MAY 21  CA/CAplus enhanced with additional kind codes for German
                  patents
 NEWS 34  MAY 22  CA/CAplus enhanced with IPC reclassification in Japanese
                  patents

 NEWS EXPRESS  NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
```

specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:35:40 ON 31 MAY 2007

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.63	0.63

FILE 'REGISTRY' ENTERED AT 11:37:06 ON 31 MAY 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 30 MAY 2007 HIGHEST RN 936211-93-7
DICTIONARY FILE UPDATES: 30 MAY 2007 HIGHEST RN 936211-93-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

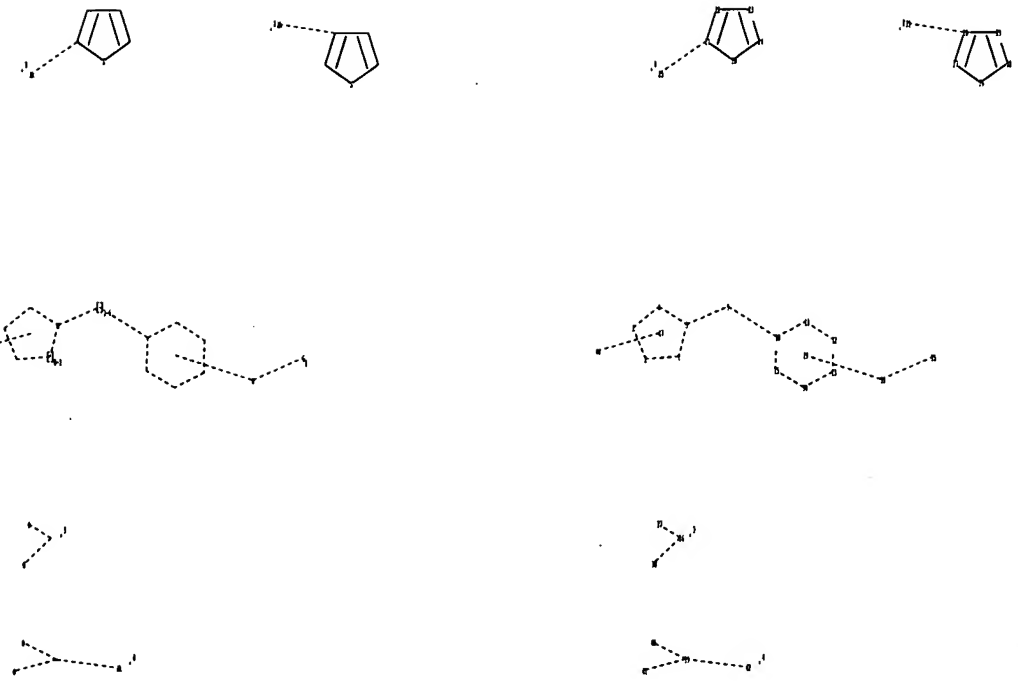
TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\QUERIES\10500895.str



chain nodes :
9 18 25 31 35 36 37 38 39 40 41 42 46
ring nodes :
1 2 3 4 5 10 11 12 13 14 15 20 21 22 23 24 26 27 28 29 30
chain bonds :
5-9 9-10 18-35 21-25 28-31 36-37 36-38 39-40 39-41 39-42
ring bonds :
1-2 1-5 2-3 3-4 4-5 10-11 10-15 11-12 12-13 13-14 14-15 20-21 20-24
21-22 22-23 23-24 26-27 26-30 27-28 28-29 29-30
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5 5-9 9-10 10-11 10-15 11-12 12-13 13-14 14-15 18-35
20-21 20-24 21-22 21-25 22-23 23-24 26-27 26-30 27-28 28-29 28-31 29-30
36-37 36-38 39-40 39-41 39-42
isolated ring systems :
containing 1 : 10 :

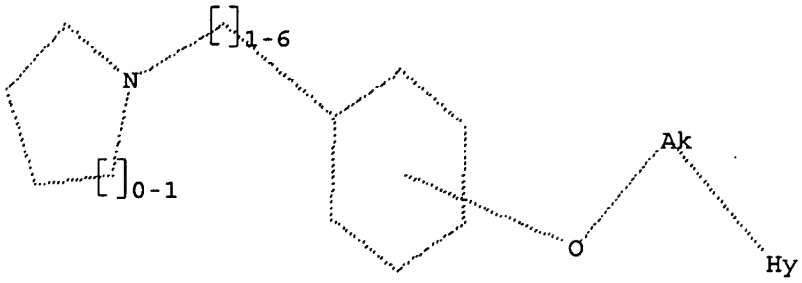
G1:[*1],[*2]

G2:[*3],[*4]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 9:CLASS 10:Atom 11:Atom 12:Atom 13:Atom
14:Atom 15:Atom 18:CLASS 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:Atom
25:CLASS 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:CLASS 35:CLASS 36:CLASS
37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:CLASS 42:CLASS 46:CLASS 47:CLASS

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

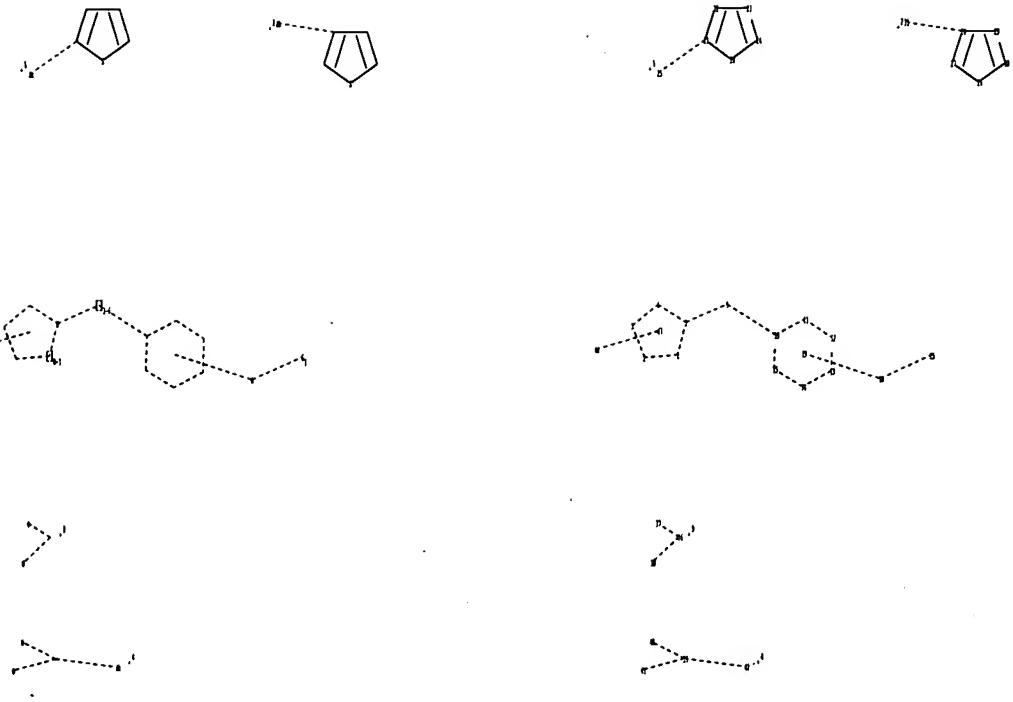
=> s l1
SAMPLE SEARCH INITIATED 11:43:17 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 443137 TO ITERATE

0.5% PROCESSED 2000 ITERATIONS 0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **INCOMPLETE**
BATCH **INCOMPLETE**
PROJECTED ITERATIONS: 8824788 TO 8900692
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=>
Uploading C:\Program Files\Stnexp\Queries\QUERIES\10500895.str



chain nodes :
9 18 25 31 35 36 37 38 39 40 41 42 46
ring nodes :
1 2 3 4 5 10 11 12 13 14 15 20 21 22 23 24 26 27 28 29 30
chain bonds :
5-9 9-10 18-35 21-25 28-31 36-37 36-38 39-40 39-41 39-42
ring bonds :
1-2 1-5 2-3 3-4 4-5 10-11 10-15 11-12 12-13 13-14 14-15 20-21 20-24
21-22 22-23 23-24 26-27 26-30 27-28 28-29 29-30
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5 5-9 9-10 10-11 10-15 11-12 12-13 13-14 14-15 18-35
20-21 20-24 21-22 21-25 22-23 23-24 26-27 26-30 27-28 28-29 28-31 29-30
36-37 36-38 39-40 39-41 39-42
isolated ring systems :
containing 1 : 10 :

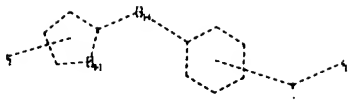
G1:[*1],[*2]

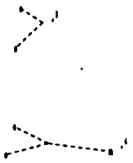
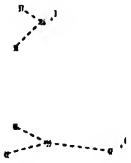
G2:[*3],[*4]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 9:CLASS 10:Atom 11:Atom 12:Atom 13:Atom
14:Atom 15:Atom 18:CLASS 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:Atom
25:CLASS 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:CLASS 35:CLASS 36:CLASS
37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:CLASS 42:CLASS 46:CLASS 47:CLASS

```
L3       STRUCTURE UPLOADED

=> d
L3 HAS NO ANSWERS
L3                STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l3
SAMPLE SEARCH INITIATED 11:44:24 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     43043 TO ITERATE

  4.6% PROCESSED      2000 ITERATIONS                                  3 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       848471 TO   873249
PROJECTED ANSWERS:             809 TO     1773

L4             3 SEA SSS SAM L3

=> s l3 full
FULL SEARCH INITIATED 11:44:31 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   859967 TO ITERATE

100.0% PROCESSED   859967 ITERATIONS                             1296 ANSWERS
SEARCH TIME: 00.00.08

L5          1296 SEA SSS FUL L3

=>
Uploading C:\Program Files\Stnexp\Queries\QUERIES\10500895.str
```





chain nodes :
9 18 25 31 35 36 37 38 39 40 41 42 46
ring nodes :
1 2 3 4 5 10 11 12 13 14 15 20 21 22 23 24 26 27 28 29 30
chain bonds :
5-9 9-10 18-35 21-25 28-31 36-37 36-38 39-40 39-41 39-42
ring bonds :
1-2 1-5 2-3 3-4 4-5 10-11 10-15 11-12 12-13 13-14 14-15 20-21 20-24
21-22 22-23 23-24 26-27 26-30 27-28 28-29 29-30
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5 5-9 9-10 10-11 10-15 11-12 12-13 13-14 14-15 18-35
20-21 20-24 21-22 21-25 22-23 23-24 26-27 26-30 27-28 28-29 28-31 29-30
36-37 36-38 39-40 39-41 39-42
isolated ring systems :
containing 1 : 10 :

G1:[*1],[*2]

G2:[*3],[*4]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 9:CLASS 10:Atom 11:Atom 12:Atom 13:Atom
14:Atom 15:Atom 18:CLASS 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:Atom
25:CLASS 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:CLASS 35:CLASS 36:CLASS
37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:CLASS 42:CLASS 46:CLASS 47:CLASS

```
L6      STRUCTURE UPLOADED

=> d
L6 HAS NO ANSWERS
L6                STR
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.


=> s l6 subset-l5 full
COMBINATION OF STRUCTURE AND TEXT TERMS NOT VALID
The query entered contains both search terms created by
structure-building or screen commands and text search terms.  L#s
created via the STRUCTURE or SCREEN commands must be searched in the
structures files separately from text terms or profiles.  The L#
answer sets from structure searches can be used in crossover searches
and can be combined with text terms.

=> s l6 subset=l5 full
FULL SUBSET SEARCH INITIATED 11:48:20 FILE 'REGISTRY'
FULL SUBSET SCREEN SEARCH COMPLETED -      506 TO ITERATE

100.0% PROCESSED      506 ITERATIONS                                27 ANSWERS
SEARCH TIME: 00.00.01

L7            27 SEA SUB=L5 SSS FUL L6

=> s l7 and caplus/lc
      54326390 CAPLUS/LC
L8           27 L7 AND CAPLUS/LC

=> fil caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   225.80     226.43

FILE 'CAPLUS' ENTERED AT 11:48:30 ON 31 MAY 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 31 May 2007  VOL 146 ISS 23
FILE LAST UPDATED: 30 May 2007  (20070530/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html
```

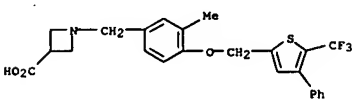
```
=> s l8
L9              8 L8

=> d ibib abs hitstr 1-8
```

L9 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:262972 CAPLUS
TITLE: Identification of Leu276 of the S1P1 receptor and Phe263 of the S1P3 receptor in interaction with receptor specific agonists by molecular modeling, site-directed mutagenesis, and affinity studies
AUTHOR(S): Deng, Qiaolin; Clemas, Joseph A.; Chrebet, Gary; Fischer, Paul; Hale, Jeffrey J.; Li, Zhen; Mills, Sander G.; Bergstrom, James; Mandala, Suzanne; Mosley, Ralph; Parent, Stephen A.
CORPORATE SOURCE: Department of Molecular Systems, Merck Research Laboratories, Rahway, NJ, USA
SOURCE: Molecular Pharmacology (2007), 71(3), 724-735
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Sphingosine-1-phosphate (S1P) receptor agonists are novel immunosuppressive agents. The selectivity of S1P1 against S1P3 is strongly correlated with lymphocyte sequestration and min. acute toxicity and bradycardia. This study describes mol. modeling, site-directed mutagenesis, and affinity studies exploring the mol. basis for selectivity between S1P1 and S1P3 receptors. Computational models of human S1P1 and S1P3 receptors bound with two nonselective agonists or two S1P1-selective agonists were developed based on the x-ray crystal structure of bovine rhodopsin. The models predict that S1P1 Leu276 and S1P3 Phe263 contribute to the S1P1/S1P3 selectivity of the two S1P1-selective agonists. These residues were subjected to site-directed mutagenesis. The wild-type and mutant S1P receptors were expressed in Chinese hamster ovary cells and examined for their abilities to bind to and be activated by agonists in vitro. The results indicate that the mutations have minimal effects on the activities of the two nonselective agonists, although they have dramatic effects on the S1P1-selective agonists. These studies provide a fundamental understanding of how these two receptor-selective agonists bind to the S1P1 and S1P3 receptors, which should aid development of more selective S1P1 receptor agonists with immunosuppressive properties and improved safety profiles.

IT 570423-80-2
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(identification of Leu276 of S1P1 receptor and Phe263 of S1P3 receptor in interaction with receptor specific agonists by mol. modeling, site-directed mutagenesis, and affinity studies)

RN 570423-80-2 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-methyl-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (CA INDEX NAME)



L9 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

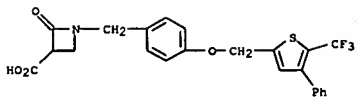
L9 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:772794 CAPLUS
DOCUMENT NUMBER: 145:369215
TITLE: Species differences in metabolism and pharmacokinetics of a sphingosine-1-phosphate receptor agonist in rats and dogs: formation of a unique glutathione adduct in the rat
AUTHOR(S): Anari, M. Reza; Creighton, Mellissa D.; Ngui, Jason S.; Tschirret-Guth, Richard A.; Teffera, Yohannes; Doss, George A.; Tang, Wei; Yu, Nathan X.; Ciccotto, Suzanne L.; Hobra, Donald F., Jr.; Coleman, John B.; Vincent, Stella H.; Evans, David C.
CORPORATE SOURCE: Department of Drug Metabolism, Merck Research Laboratories, West Point, PA, USA
SOURCE: Drug Metabolism and Disposition (2006), 34(8), 1367-1375
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The pharmacokinetics and metabolism of 1-(4-((4-phenyl-5-trifluoromethyl-2-thienyl)methoxy)benzyl)azetidine-3-carboxylic acid (MRL-A), a selective agonist for the sphingosine-1-phosphate 1 (S1P1) receptor, were investigated in rats and dogs. In both species, more than 50% of the dose was excreted in bile. Specific to the rat, and observed in bile, were a taurine conjugate of MRL-A and a glucuronide conjugate of an azetidine lactam metabolite. In dogs, a smaller portion of the dose (54% of administered dose) was excreted intact in bile, and the major metabolites detected were an azetidine N-oxide of MRL-A and an acylglucuronide of an N-dealkylation product. This latter metabolite was also observed in rat bile. Stereoselective formation of the N-oxide isomer was observed in dogs, whereas the rat produced comparable amts. of both isomers. The formation of a unique glutathione adduct was observed in rat bile, which was proposed to occur via N-dealkylation, followed by reduction of the putative aldehyde product to form the alc., and dehydration of the alc. to generate a reactive quinone methide intermediate. Incubation of a synthetic standard of this alc. in rat microsomes fortified with reduced glutathione or rat hepatocytes resulted in formation of this unique glutathione adduct.

IT 910579-67-8 910579-68-9 910579-72-5
910582-20-6
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(species differences in metabolism and pharmacokinetics of a sphingosine-1-phosphate receptor agonist MRL-A in rats and dogs)

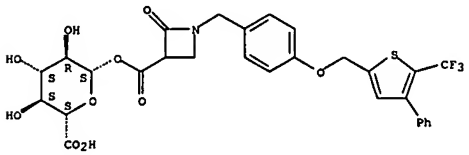
RN 910579-67-8 CAPLUS
CN 3-Azetidinecarboxylic acid, 2-oxo-1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

L9 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

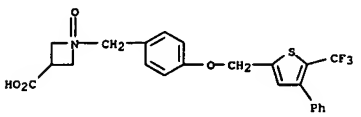


RN 910579-68-9 CAPLUS
CN β-D-Glucopyranuronic acid, 1-[2-oxo-1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]-3-azetidinecarboxylate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

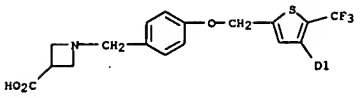


RN 910579-72-5 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]-, 1-oxide (9CI) (CA INDEX NAME)

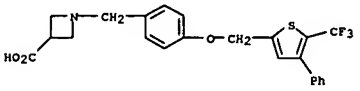


RN 910582-20-6 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[4-[[4-[(sulfooxy)phenyl]-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

L9 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

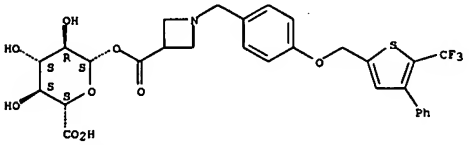


IT 570423-67-5, MRL-A
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(species differences in metabolism and pharmacokinetics of a sphingosine-1-phosphate receptor agonist MRL-A in rats and dogs)
RN 570423-67-5 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



IT 910579-73-6
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(species differences in metabolism andpharmacokinetics of a sphingosine-1-phosphate receptor agonist MRL-A in rats and dogs)
RN 910579-73-6 CAPLUS
CN β-D-Glucopyranuronic acid, 1-[1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]-3-azetidinecarboxylate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



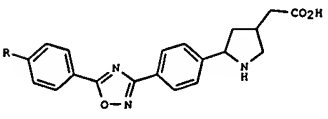
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS

L9 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE

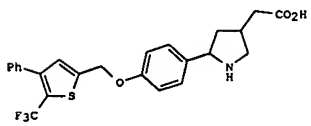
FORMAT

L9 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:499151 CAPLUS
DOCUMENT NUMBER: 145:145483
TITLE: 2-Aryl(pyrrolidin-4-yl)acetic acids are potent agonists of sphingosine-1-phosphate (S1P) receptors
AUTHOR(S): Yan, Lin; Budhu, Richard; Huo, Pei; Lynch, Christopher L.; Hale, Jeffrey J.; Mills, Sander G.; Hajdu, Richard; Keohane, Carol A.; Rosenbach, Mark J.; Milligan, James A.; Shei, Gan-Ju; Chrebet, Gary; Bergstrom, James; Card, Deborah; Mandala, Suzanne M.
CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(13), 3564-3568
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:145483
GI



I

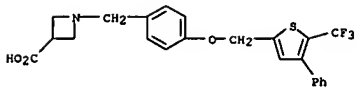


II

AB 2-Aryl(pyrrolidin-4-yl)acetic acids I (R = i-Bu, cyclopentyl, cyclohexyl, F3C(CH2)2, 3,3-difluoro-1-cyclopentyl, 4,4-difluoro-1-cyclohexyl) and II were synthesized and their biol. activities as agonists of S1P receptors were evaluated. These analogs were able to induce lowering of lymphocyte counts in the peripheral blood of mice and were found to have good overall pharmacokinetic properties in rats.

IT 570423-67-5
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); BIOL (Biological study)
(preparation and biol. activity of thiophene- or oxadiazole-functionalized (aryl)pyrrolidineacetic acids as potent agonists of sphingosine-1-phosphate receptors)
RN 570423-67-5 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

L9 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

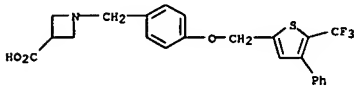
L9 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:986123 CAPLUS
DOCUMENT NUMBER: 143:431986
TITLE: Discovery of Potent 3,5-Diphenyl-1,2,4-oxadiazole Sphingosine-1-phosphate-1 (S1P1) Receptor Agonists with Exceptional Selectivity against S1P2 and S1P3
AUTHOR(S): Li, Zhen; Chen, Weirong; Hale, Jeffrey J.; Lynch, Christopher L.; Mills, Sander G.; Hajdu, Richard; Keohane, Carol Ann; Rosenbach, Mark J.; Milligan, James A.; Shei, Gan-Ju; Chrebet, Gary; Parent, Stephen A.; Bergstrom, James; Card, Deborah; Forrest, Michael; Quackenbush, Elizabeth J.; Wickham, L. Alexandra; Vargas, Hugo; Evans, Rose M.; Rosen, Hugh; Mandala, Suzanne
CORPORATE SOURCE: Departments of Medicinal Chemistry and Immunology Rheumatology Research, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Journal of Medicinal Chemistry (2005), 48(20), 6169-6173
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:431986

AB A class of 3,5-diphenyl-1,2,4-oxadiazole based compds. have been identified as potent sphingosine-1-phosphate-1 (S1P1) receptor agonists with minimal affinity for the S1P2 and S1P3 receptor subtypes. Analog 26 (S1P1 IC50 = 0.6 nM) has an excellent pharmacokinetics profile in the rat and dog and is efficacious in a rat skin transplant model, indicating that S1P3 receptor agonism is not a component of immunosuppressive efficacy.

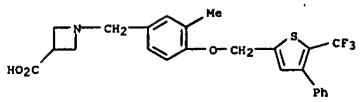
IT 570423-67-5 570423-80-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Discovery of Potent 3,5-Diphenyl-1,2,4-oxadiazole Sphingosine-1-phosphate-1 (S1P1) Receptor Agonists with Exceptional Selectivity)

RN 570423-67-5 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 570423-80-2 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-methyl-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (CA INDEX NAME)

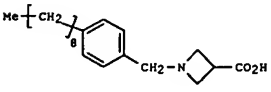
L9 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:1048937 CAPLUS
DOCUMENT NUMBER: 142:147835
TITLE: A Rational Utilization of High-Throughput Screening Affords Selective, Orally Bioavailable 1-Benzyl-3-carboxyazetidine Sphingosine-1-phosphate-1 Receptor Agonists
AUTHOR(S): Hale, Jeffrey J.; Lynch, Christopher L.; Neway, William; Mills, Sander G.; Hajdu, Richard; Keohane, Carol Ann; Rosenbach, Mark J.; Milligan, James A.; Shei, Gan-Ju; Parent, Stephen A.; Chrebet, Gary; Bergstrom, James; Card, Deborah; Ferrer, Marc; Hodder, Peter; Strulovici, Berta; Rosen, Hugh; Mandala, Suzanne
CORPORATE SOURCE: Departments of Medicinal Chemistry and Immunology and Rheumatology Research, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Journal of Medicinal Chemistry (2004), 47(27), 6662-6665
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:147835
GI



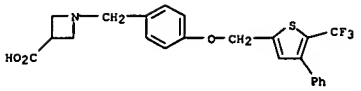
I

AB Moderately potent, selective S1P1 receptor agonists identified from high-throughput screening have been adapted into lipophilic tails for a class of orally bioavailable amino acid-based S1P1 agonists represented by I. Many of the new compds. are potent S1P1 agonists that select against the S1P2, S1P3, and S1P4 (although not S1P5) receptor subtypes. Two of the analogs are highly orally bioavailable and possess excellent pharmacokinetic profiles in the rat, dog, and rhesus monkey.

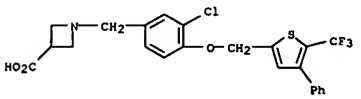
IT 570423-67-5P 570423-76-6P 570423-80-2P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(1-benzyl-3-carboxyazetidine derivs. as EDG-1 receptor agonists and immunosuppressants: high-throughput screening for oral bioavailability and preparation)

RN 570423-67-5 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

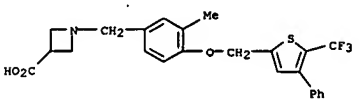
L9 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 570423-76-6 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-chloro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

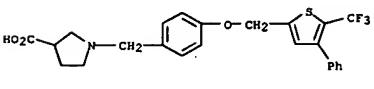


RN 570423-80-2 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-methyl-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (CA INDEX NAME)



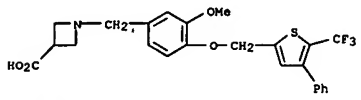
IT 570423-45-9P 570423-78-8P 828269-16-5P 828269-17-6P 828269-18-7P 828269-19-8P 828269-20-1P 828269-21-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(1-benzyl-3-carboxyazetidine derivs. as EDG-1 receptor agonists and immunosuppressants: high-throughput screening for oral bioavailability and preparation)

RN 570423-45-9 CAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

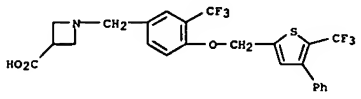


L9 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

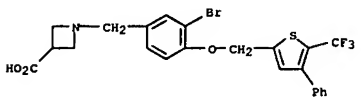
RN 570423-78-8 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-methoxy-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



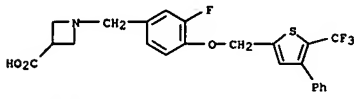
RN 828269-16-5 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]-3-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



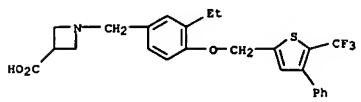
RN 828269-17-6 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-bromo-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



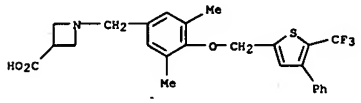
RN 828269-18-7 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-fluoro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



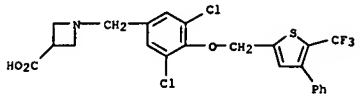
RN 828269-19-8 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-ethyl-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 828269-20-1 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3,5-dimethyl-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 828269-21-2 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3,5-dichloro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



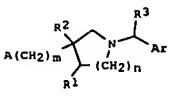
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:591193 CAPLUS
DOCUMENT NUMBER: 139:149520
TITLE: Preparation of aralkylpyrrolidines and -azetidines as Edg receptor agonists
INVENTOR(S): Bugianesi, Robert L.; Doherty, George A.; Gentry, Amy; Hale, Jeffrey J.; Lynch, Christopher L.; Mills, Sander G.; Neway, William E., III
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003062252	A1	20030731	WO 2003-US1196	20030115
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2472715	A1	20030731	CA 2003-2472715	20030115
EP 1470137	A1	20041027	EP 2003-705779	20030115
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005515259	T	20050526	JP 2003-562129	20030115
US 2005033055	A1	20050210	US 2004-500895	20040707
PRIORITY APPLN. INFO.:			US 2002-350000P	P 20020118
			WO 2003-US1196	W 20030115

OTHER SOURCE(S): MARPAT 139:149520
GI

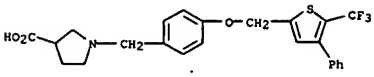


I

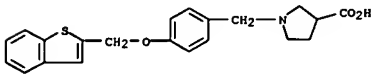
AB Title compds. I [Ar = (un)substituted Ph, naphthyl; A = CO2H, P(O)(OH)2, P(O)OH, SO3H, 1H-tetrazol-5-yl; R1, R2 = H, halogen, OH, CO2H, (un)substituted alkyl; R3 = H, (un)substituted alkyl; m, n = 0, 1] were prepared for use as Edg receptor agonists, useful for treating immune mediated diseases and conditions, such as bone marrow, organ and tissue transplant rejection (no data). Thus, 3-pyrrolidinol was converted to di-Et 3-hydroxypyrrolidin-3-ylphosphonate and treated with 4-nonylbenzaldehyde, followed by ester hydrolysis to give 1-(4-nonylbenzyl)-3-hydroxypyrrolidine-3-phosphonic acid.

IT 570423-45-9P 570423-58-4P 570423-65-3P 570423-67-5P 570423-73-3P 570423-74-4P 570423-75-5P 570423-76-6P 570423-77-7P 570423-78-8P 570423-79-9P 570423-80-2P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aralkylpyrrolidines and -azetidines as Edg receptor agonists)

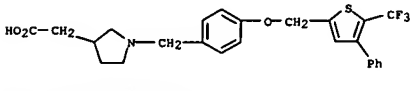
RN 570423-45-9 CAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



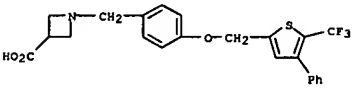
RN 570423-58-4 CAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[[4-(benzo[b]thien-2-ylmethoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 570423-65-3 CAPLUS
CN 3-Pyrrolidineacetic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

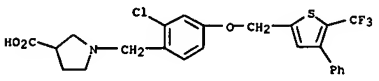


RN 570423-67-5 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

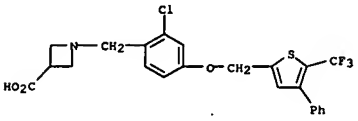


L9 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

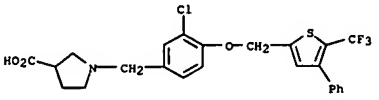
RN 570423-73-3 CAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[[2-chloro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



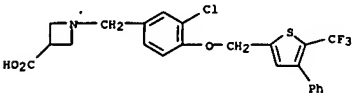
RN 570423-74-4 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[2-chloro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 570423-75-5 CAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[[3-chloro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



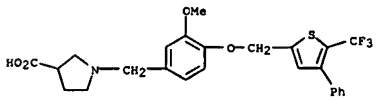
RN 570423-76-6 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-chloro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



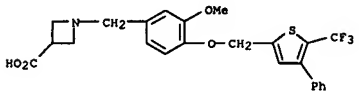
L9 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

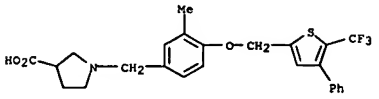
RN 570423-77-7 CAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[[3-methoxy-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



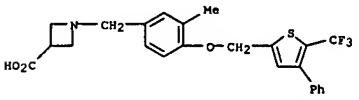
RN 570423-78-8 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-methoxy-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 570423-79-9 CAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[[3-methyl-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 570423-80-2 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-methyl-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

L9 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:590932 CAPLUS
DOCUMENT NUMBER: 139:149413
TITLE: Selective S1P1/Edg1 receptor agonists
INVENTOR(S): Doherty, George A.; Forrest, Michael J.; Hajdu, Richard; Hale, Jeffrey J.; Li, Zhen; Mandala, Suzanne M.; Mills, Sander G.; Rosen, Hugh; Scolnick, Edward M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 202 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003061567	A2	20030731	WO 2003-US1120	20030114
WO 2003061567	A3	20031224		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004058894	A1	20040325	US 2003-339380	20030109
CA 2472680	A1	20030731	CA 2003-2472680	20030114
EP 1469863	A2	20041027	EP 2003-731917	20030114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005070506	A1	20050331	US 2004-501176	20040712

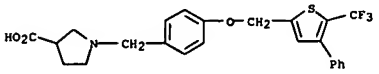
PRIORITY APPLN. INFO.:
US 2002-349991P P 20020118
US 2002-362566P P 20020307
US 2002-382933P P 20020523
WO 2003-US1120 W 20030114

AB The present invention encompasses a method of treating an immunoregulatory abnormality in a mammalian patient in need of such treatment comprising administering to said patient a compound which is an agonist of the S1P1/Edg1 receptor in an amount effective for treating said immunoregulatory abnormality, wherein said compound possesses a selectivity for the S1P1/Edg1 receptor over the S1PR3/Edg3 receptor, said compound administered in an amount effective for treating said immunoregulatory abnormality. Thus, 4-HOC6H4CHO was treated with Me(CH2)7I to give 4-Me(CH2)7OC6H4CHO which was treated with H2N(CH2)3P(O)(OH)2 to give 4-Me(CH2)7OC6H4CH2NH(CH2)3P(O)(OH)2 which had an EC50 for S1P1 agonism of 1.5 nM and for S1P3 agonism of 6.0 nM.

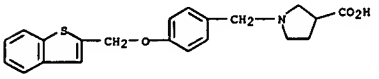
IT 570423-45-9P 570423-58-4P 570423-65-3P 570423-67-5P 570423-73-3P 570423-74-4P

L9 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
570423-75-5P 570423-76-6P 570423-77-7P
570423-78-8P 570423-79-9P 570423-80-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

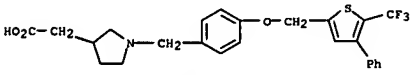
RN 570423-45-9 CAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



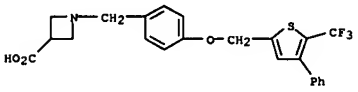
RN 570423-58-4 CAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[[4-(benzo[b]thien-2-ylmethoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 570423-65-3 CAPLUS
CN 3-Pyrrolidineacetic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

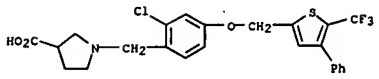


RN 570423-67-5 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

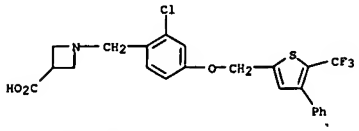


RN 570423-73-3 CAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[[2-chloro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

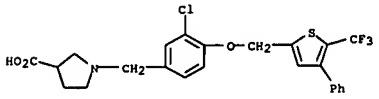
L9 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



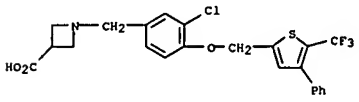
RN 570423-74-4 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[2-chloro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 570423-75-5 CAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[[3-chloro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

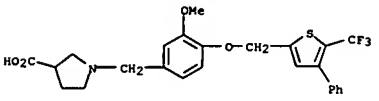


RN 570423-76-6 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-chloro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

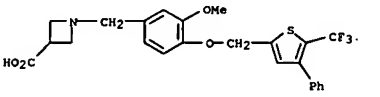


RN 570423-77-7 CAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[[3-methoxy-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

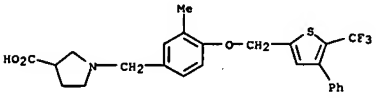
L9 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



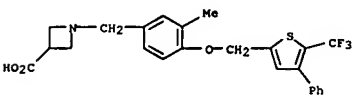
RN 570423-78-8 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-methoxy-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 570423-79-9 CAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[[3-methyl-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 570423-80-2 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-methyl-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

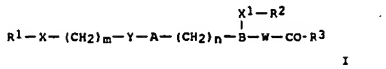
ACCESSION NUMBER: 2001:396864 CAPLUS
DOCUMENT NUMBER: 135:19632
TITLE: Preparation of pyrazolyl- and pyrrolylalkanoic acid derivatives with hypoglycemic and hypolipidemic activity
INVENTOR(S): Momose, Yu; Maekawa, Tsuyoshi; Odaka, Hiroyuki; Kimura, Hiroyuki
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 375 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001038325	A1	20010531	WO 2000-JP7877	20001109
W: AE, AG, AL, AM, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2390923	A1	20010531	CA 2000-2390923	20001109
JP 2001226350	A	20010821	JP 2000-347462	20001109
JP 3723071	B2	20051207		
BR 2000015466	A	20020806	BR 2000-15466	20001109
EP 1228067	A1	20020807	EP 2000-974857	20001109
EP 1228067	B1	20040714		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 200203165	A2	20030128	HU 2002-3165	20001109
JP 2003137865	A	20030514	JP 2002-315096	20001109
NZ 519238	A	20031128	NZ 2000-519238	20001109
AT 271049	T	20040715	AT 2000-974857	20001109
EP 1457490	A1	20040915	EP 2004-76508	20001109
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PT 1228067	T	20041130	PT 2000-974857	20001109
ES 2225252	T3	20050316	ES 2000-974857	20001109
AU 780948	B2	20050428	AU 2001-13031	20001109
RU 2252939	C2	20050527	RU 2002-115263	20001109
NO 2002002108	A	20020708	NO 2002-2108	20020502
US 7179823	B1	20070220	US 2002-129702	20020509
IN 2002KN00645	A	20050311	IN 2002-KN645	20020513
ZA 2002003824	A	20031015	ZA 2002-3824	20020514
HK 1045991	A1	20041210	HK 2002-106297	20020827

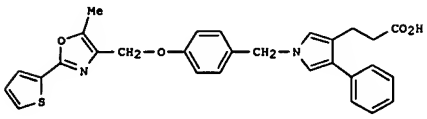
PRIORITY APPLN. INFO.:

JP 1999-320317	A	19991110
JP 1999-352237	A	19991210
JP 1999-352236	A	19991210
EP 2000-974857	A3	20001109
JP 2000-347462	A3	20001109
WO 2000-JP7877	W	20001109

L9 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
OTHER SOURCE(S): MARPAT 135:19632
GI



I

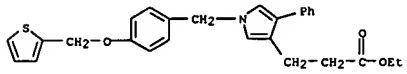


II

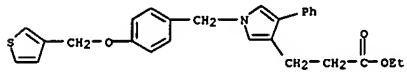
AB Title compds. (I) [wherein R1 = (un)substituted hydrocarbon or heterocycle; X = bond, O, S, CO, CS, CR4(OR5), or NR6; R4 and R6 = independently H or (un)substituted hydrocarbon; R5 = H or hydroxyl protective group; m = 0-3; Y = O, S, SO, SO2, NR7, CONR7, or NR7CO; R7 = H or (un)substituted hydrocarbon; A = (un)substituted aromatic ring; n = 1-8; B = (un)substituted N-containing 5-membered heterocycle; X1 = bond, O, S, SO, SO2, OSO2, or NR16; R16 = H or (un)substituted hydrocarbon; R2 = H or (un)substituted hydrocarbon or heterocycle; W = bond or hydrocarbon; R3 = OR8 or NR9R10; R8 = H or (un)substituted hydrocarbon; R9 and R10 = independently H or (un)substituted hydrocarbon or heterocycle; or R9 and R10 together with the N to which they are attached may form a ring] were prepared as retinoid-related receptor function regulating agents or insulin resistance improving agents. For example, Et 3-[1-(4-hydroxybenzyl)-4-phenyl-3-pyrrolyl]propionate and 4-chloromethyl-5-methyl-2-(2-thienyl)oxazole were coupled in the presence of K2CO3 in DMF and treated with HCl to give II (77%). At a concentration of 0.001%, II reduced hypoglycemic and hypolipidemic action by 48% and 70%, resp., lowered total cholesterol by 16%, and increased the plasma anti-arteriosclerosis index by 12% compared to non-treatment groups of mice. In addition, II showed potent PPARγ-RXRα heterodimer ligand activity with EC50 of 1.5 nM. I are useful for the prevention or treatment of diabetes mellitus, hyperlipidemia, impaired glucose tolerance, inflammatory diseases, and arteriosclerosis.

IT 342025-29-0P 342025-31-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of pyrrolyl- and pyrazolylalkanoic acid derivs. as retinoid X receptor and PPAR receptor modulators)

RN 342025-29-0 CAPLUS
CN 1H-Pyrrole-3-propanoic acid, 4-phenyl-1-[[4-(2-thienylmethoxy)phenyl]methyl]-, ethyl ester (9CI) (CA INDEX NAME)

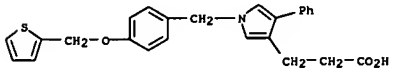


RN 342025-31-4 CAPLUS
CN 1H-Pyrrole-3-propanoic acid, 4-phenyl-1-[[4-(3-thienylmethoxy)phenyl]methyl]-, ethyl ester (9CI) (CA INDEX NAME)

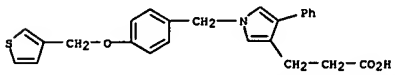


IT 342025-30-3P 342025-32-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolyl- and pyrazolylalkanoic acid derivs. as retinoid X receptor and PPAR receptor modulators)

RN 342025-30-3 CAPLUS
CN 1H-Pyrrole-3-propanoic acid, 4-phenyl-1-[[4-(2-thienylmethoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 342025-32-5 CAPLUS
CN 1H-Pyrrole-3-propanoic acid, 4-phenyl-1-[[4-(3-thienylmethoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	42.63	269.06

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-6.24	-6.24

STN INTERNATIONAL LOGOFF AT 11:48:53 ON 31 MAY 2007